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The application was originally filed in English.

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For the Patent- and Registration Office

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Anita Södervall

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NEW MEASURING TECHNIQUE

Field of invention

The present invention relates to a method of analysing a turbid pharmaceutical sample, e.g. a tablet, a capsule - especially a multiple unit pellet system (MUPS) tablet or capsule - or a similar sample forming a pharmaceutical dose. The invention also relates to an apparatus for performing such a method.

The present invention can be combined with the invention and the spectrometric methods and set-ups as disclosed in applicant's copending International patent application PCT/SE99/00463 filed before the present application but unpublished on the filing date of the present application. Especially, the present invention can be combined with the technique disclosed therein for irradiating two opposite surfaces of an analysed sample, in order to obtain signals representative of the three-dimensional distribution of at least one component in the sample. The content of this International patent application is hereby incorporated by reference.

Background of the invention

Non-invasive, non-destructible analysis of whole tablets can be carried out by means of near-infrared (NIR) or Raman spectrometry. Today, NIR spectroscopy is a recognised technique for performing a fast analysis of compounds. The common feature of both these techniques is that they utilise light in the NIR wavelength region (700-2500 nm, specifically 700-1500 nm) where pharmaceutical tablets are relatively transparent (low molar absorptivity). That is, light can in this region penetrate compressed powders several mm:s why information on the content can be obtained emanating from the bulk of the tablet and not only from the surface. A practical advantage of using NIR radiation is that diode lasers can be used.

One example of such an analysis is described in US 5 760 399, assigned to Foss NIRsystems Inc. This document discloses an instrument for performing a NIR spectrographic transmission measurement of a pharmaceutical tablet. This instrument is, however, capable of providing only limited information as to the content of a sample, typically the quantity of a particular component in a sample. This prior-art instrument cannot provide detailed information of, for example, the three-dimensional distribution of

one or more components in a sample. The technical background on which this limitation is based will be further discussed in connection with the description of the present invention.

The prior art also includes a significant amount of methods for optical imaging of human tissues, in particular for detecting disturbances of homogeneity, such as the presence of a tumour in a human tissue. These methods are generally qualitative measurements, not quantitative, in the sense that they primarily focus on determining the presence and the location of an inhomogeneity. These prior-art methods are not suitable for performing a quantitative analysis on pharmaceutical, turbid samples, such as tablets and capsules, in order to determine e.g. content and structural parameters.

Summary of the invention

According to a first aspect of the invention there is provided a method for use in quantitative analysis of a turbid, pharmaceutical sample, in particular a pharmaceutical tablet, capsule of an equivalent pharmaceutical dose.

According to the invention, the method comprises the following steps:

- providing an excitation beam of radiation;
- irradiating a pharmaceutical, turbid sample with said excitation beam of radiation; and
- measuring the intensity of emitted radiation from the thus irradiated sample as a function of both the wavelength of the emitted radiation and the photon propagation time through said sample.

The invention is based on the following principles. A sample to be analysed by a spectrometric transmission and/or reflection measurement presents a number of so called optical properties. These optical properties are (i) the absorption coefficient, (ii) the scattering coefficient and (iii) the scattering anisotropy. Thus, when the photons of the excitation beam propagate through the turbid sample – in transmission and/or reflection mode - they are influenced by these optical properties and, as a result, subjected to both absorption and scattering. Photons that by coincidence travel along an essentially straight path through the sample and thus do not experience any appreciable scattering will exit the sample with a relatively short time delay. Photons that are directly reflected on the irradiated surface will also present a relatively short time delay, in the case of measurements on reflected light. On the other hand, highly scattered photons (transmitted and/or reflected) exit with a substantial time delay. This means that all these emitted

photons – presenting different propagation times - mediate complementary information about the sample.

In a conventional steady state (no time-resolution) measurement, some of that complementary information is added together since the emitted light is captured by a time-integrated detection. Accordingly, the complementary information is lost in a conventional technique. For instance, a decrease in the registered light intensity may be caused by an increase in the sample absorption coefficient, but it may also be caused by a change in the sample scattering coefficient. However, the information about the actual cause is hidden, since all the emitted light has been time-integrated.

According to the invention and in contrast to such prior-art NIR spectroscopy with time-integrated intensity detection, the intensity of the emitted radiation from the sample is measured both as a function of the wavelength and as a function of the photon propagation time through said sample. Thus, the inventive method can be said to be both wavelength-resolved and time-resolved. It is important to note that the method is time-resolved in the sense that it provides information about the kinetics of the radiation interaction with the sample. Thus, in this context, the term "time resolved" means "photon propagation time resolved". In other words, the time resolution used in the invention is in a time scale which corresponds to the photon propagation time in the sample (i.e. the photon transit time from the source to the detector) and which, as a consequence, makes it possible to avoid time-integrating the information relating to different photon propagation times. As an illustrative example, the transit time for the photons may be in the order of 0,1-2 ns. Especially, the term "time resolved" is not related to a time period necessary for performing a spatial scanning, which is the case in some prior-art NIR-techniques where "time resolution" is used.

As a result of not time-integrating the radiation (and thereby "hiding" a lot of information) as done in the prior art, but instead time resolving the information from the excitation of the sample in combination with wavelength resolving the information, the invention makes it possible to establish quantitative analytical parameters of the sample, such as content, concentration, structure, homogeneity, etc.

Both the transmitted radiation and the reflected radiation from the irradiated sample comprise photons with different time delay. Accordingly, the time-resolved and wavelength resolved detection may be performed on transmitted radiation only, reflected radiation only, as well as a combination of transmitted and reflected radiation.

The excitation beam of radiation used in the present invention may include infrared radiation, especially near infrared (NIR) radiation of in the range corresponding to wavelengths of from about 700 to about 1700 nm, particularly from 700 to 1300 nm. However, the excitation beam of radiation may also include visible light (400 to 700 nm) and UV radiation. In this connection, it should also be stated that the term "excitation" should be interpreted as meaning "illumination", i.e. no chemical excitation of the sample is necessary.

Preferably, the step of measuring the intensity as a function of photon propagation time is performed in time-synchronism with the excitation of the sample. In a first preferred embodiment, this time synchronism is implemented by using a pulsed excitation beam, presenting a pulse train of short excitation pulses, wherein each excitation pulse triggers the intensity measurement. To this end, a pulsed laser system or laser diodes can be used. This technique makes it possible to perform a photon propagation time-resolved measurement of the emitted intensity (transmitted and/or reflected) for each given excitation pulse, during the time period up to the subsequent excitation pulse.

In order to avoid any undesired interference between the intensity measurements relating to two subsequent excitation pulses, such excitation pulses should have a pulse length short enough in relation to the photon propagation time in the sample and, preferably, much shorter than the photon propagation time.

To summarise, in this embodiment of the invention the intensity detection of the emitted radiation associated with a given excitation pulse is time-synchronised with this pulse, and the detection of the emitted light from one pulse is completed before the next pulse.

The data evaluation can be done in different ways. By defining the boundary conditions and the optical geometry of the set-up, iterative methods such as Monte Carlo simulations can be utilised to calculate the optical properties of the sample and indirectly content and structural parameters. Alternatively, a multivariate calibration can be used for a direct extraction of such parameters. In multivariate calibration, measured data is utilised to establish an empirical mathematical relationship to the analytical parameter of interest, such as the content or structure of a pharmaceutical substance. When new measurements are performed, the model can be used to predict the analytical parameters of the unknown sample.

In an alternative embodiment the radiation source is intensity modulated in time. Then, frequency domain spectroscopy can be used for determining phase shift and/or modulation

depth of the emitted radiation from the sample. Thus, the phase and/or modulation depth of the emitted sample radiation is compared with those of the excitation radiation. That information can be used to extract information about the time delay of the radiation in the sample. It should be noted that such a frequency domain spectroscopy is also a "time-resolved" technique according to the invention, since it also provides information about the kinetics of the photon interaction with the sample. With similar mathematical procedures as above, the same quantitative analytical information can be extracted.

A pulsed excitation beam according to the first embodiment, and an intensity modulated excitation beam according to the second embodiment, share the common feature that they make it possible to identify – in said excitation beam - a specific "excitation time point" which can be used to trigger the detection of the emitted radiation from the sample, i.e. to time-synchronise the time-resolved detection with the excitation of the sample. This can be performed by letting the pulsed or modulated beam trigger a photodetector or the equivalent, which in its turn triggers the detection unit via suitable time-control circuitry.

The time-resolved detection may be implemented by the use of a time-resolved detector, such as a streak camera. It may also be implemented by the use of a time-gated system, by which the detection of emitted radiation is performed during a limited number of very short time slices instead of the full time course. The time length of each such time slice is only a fraction of the detection time period during which the time resolved detection is performed for each excitation. By measuring several such "time slices" a coarse time resolution is achieved. An attractive alternative is to measure wavelength resolved spectra at two such time gates, prompt light and delayed light. Furthermore, time-resolved data may be recorded by means of other time-resolved equipment, transient digitizers or equivalent.

The wavelength-resolved detection may be implemented in many different, conventional ways. It may be implemented by the use of one or more single-channel detectors for selecting one or more wavelengths, such as ultrafast photo diodes, photomultipliers, etc, or by the use of a multi-channel detector, such as a microchannel plates or a streak camera. Use can be made of light dispersive systems, such as (i) a spectrometer, (ii) a wavelength dependent beam splitter,(iii) a non-wavelength dependent beam splitter in combination with a plurality of filters for filtering each of respective components for providing radiation of different wavelength or wavelength band, (iv) a prism array or a lens system separating the emitted radiation from the sample into a plurality of components in combination with a plurality of filters, etc.

In accordance with a further aspect of the invention, there is also provided an apparatus for performing the inventive method, said apparatus having the features as defined in the enclosed claims.

The above and other features and advantages of the invention are defined in the claims and described in greater detail below with reference to the accompanying drawings, which illustrate preferred embodiments.

Description of the drawings

Fig. 1a illustrates a set-up for performing a time-resolved and wavelength-resolved analysis according to the invention.

Fig. 1b illustrates an embodiment where the excitation and the collection of emitted light are performed at the irradiation side only of the sample.

Fig. 2 illustrates functional components for implementing the present invention.

Fig. 3a is a streak camera image, illustrating an experimental result of a wave-length-resolved and time-resolved tablet transmission measurement according to the invention.

Fig. 3b is a 3D plot of the streak camera image in Fig. 3a.

Fig. 4a is a streak camera image, illustrating an experimental result of a time-resolved tablet transmission measurement according to the invention, in combination with spatial resolution.

Fig. 4b is a 3D plot of the streak camera image in Fig. 4a.

Fig. 5 is a diagram illustrating experimental results from transmission measurements on two different tablet samples.

Description of preferred embodiments

Referring now to Fig. 1a, an apparatus according to a first embodiment for performing a time-resolved analysis according to the invention comprises a TI:saphire laser 10 pumped by an argon ion laser 12. The laser beam 14 thereby generated is amplified by a neodymium YAG amplifier stage 16 into an amplified laser beam 18. In order to create an

excitation beam 20 of "white" light, the laser beam 18 is passed through a water filled cuvette 22 via a mirror M1 and a first lens system L1.

A sample to be analysed is schematically illustrated at reference numeral 24 and comprises a front surface 26 and a back surface 28. The sample 24 is temporarily fixed in a sample positioning unit (not shown). The excitation laser beam 20 is focused onto the front surface 26 of sample 24 via a lens system L2/L3 and mirrors M2-M4. On the opposite side of sample 24, the transmitted laser beam 30 is collected from the backside by lens system L4/L5 and focused into a spectrometer 32. In the illustrated set-up, the sample 24 may be a pharmaceutical, solid tablet having a diameter of e.g. 9 mm. The excitation beam 20 may be focused on a spot of about 1 mm. In other embodiments, the excitation beam may be focused on the whole sample, or scanned over the sample.

As schematically illustrated in Fig. 1a, the excitation beam 20 in this embodiment is time-pulsed into a pulse train of short, repetitive excitation pulses P. The pulse length of each excitation pulse P is short enough and the time spacing between two consecutive excitation pulses P is long enough in relation to the transit time of the beam (i.e. in relation to the time taken for each pulse to be completely measured in time), such that any interference is avoided between the detected light from one given excitation pulse P_n and the detected light from the next excitation pulse P_{n+1}. Thereby, it is possible to perform a time-resolved measurement on the radiation from one excitation pulse P at a time.

From the spectrometer 32, the detected light beam 33 is passed via lens system L6/L7 to a time-resolved detection unit, which in this embodiment is implemented as a streak camera 34. The streak camera 34 used in an experimental set-up according to Fig. 1 was a Hamamutsu Streak Camera Model C5680. Specifically, the streak camera 34 has an entrance slit (not shown) onto which the detected light beam 33 from the spectrometer 32 is focused. It should be noted that only a fraction of the light emitted from the sample is actually collected in the spectrometer 32 and, thereby, in the detection unit 34. As a result of passing through the spectrometer 32, the emitted radiation 30 from the sample 24 is spectrally divided in space, such that radiation received by the streak camera 34 presents a wavelength distribution along the entrance slit.

The incecent photons at the slit are converted by the streak camera into photoelectrons and accelerated in a path between pairs of deflection plates (not shown). Thereby, the photoelectrons are swept along an axis onto a microchannel plate inside the camera, such that the time axis of the incident photons is converted into a spatial axis on said microchannel plate. Thereby, the time in which the photons reached the streak camera and

the intensity can be determined by the position and the luminance of the streak image. The wavelength-resolution is obtained along the other axis. The photoelectron image is read out by a CCD device 36, which is optically coupled to the streak camera 34. The data collected by the CCD device 36 is coupled to an analysing unit 38, schematically illustrated as a computer and a monitor.

In the set-up in fig. 1a, the intensity of the emitted light is measured as a function of time in time-synchronism with each excitation of the sample. This means that the detection unit comprising the streak camera 34 and the associated CCD device 36 is time-synchronised with the repetitive excitation pulses P. This time-synchronism is accomplished as follows: each excitation pulse P of the laser beam 14 triggers a photodetector 42 or the equivalent via an optical element 40. An output signal 43 from the photodetector 42 is passed via a delay generator 44 to a trig unit 46, providing trig pulses to the streak camera 34. In this manner, the photon detection operation of the streak camera is activated and de-activated at exact predetermined points of time after the generation of each excitation pulse P.

As mentioned above, the evaluation and analyse of the collected, time-resolved information can be done in different ways. As schematically illustrated in Fig. 1, the collected data information from each excitation is transferred from the streak camera 34 and the CCD device 36 to a computer 38 for evaluation of the information. Monte Carlo simulations, multivariate calibrations, etc as mentioned in the introductory part of this application can be utilised in order to calculate the optical properties of the sample and, indirectly, content and structural parameters of the sample 24.

In the embodiment shown in Fig. 1b, it is the transmitted radiation – the beam 30 – which is detected in a time-resolved manner. However, the invention can also be implemented by detecting the radiation reflected from the sample. Fig. 1b schematically illustrates how an excitation beam 20' corresponding to excitation beam 20 in Fig. 1 is focused via a lens L3' onto the front surface 26 of a sample 24. The photons of each excitation pulse will be reflected both as directly reflected photons from the front surface 26 as well as diffusely backscattered photons with more or less time delay. This directly reflected radiation as well as the diffusely backscattered radiation is collected by a lens L4' into a detection beam 30', corresponding to detection beam 30 in Fig. 1.

As stated above, it is possible to combine the embodiments illustrated in Figs 1a and 1b into one single embodiment, where both transmitted and backscattered light is detected and analysed in a time-resolved and wavelength-resolved manner according to the invention.

Fig. 2 schematically discloses the main functional components in an embodiment for implementing the inventive method, including a radiation generation unit 100 (components 10, 12 and 16 in Fig. 1a), a sample positioning unit 102, one or more wavelength dispersive/selective elements 104 (component 32 in Fig. 1a), one or more detector units 106 (components 34 and 36) in Fig. 1a) and an analysing unit 108 (component 38 in Fig. 1a).

The water filled cuvette 22 producing white laser light in combination with the spectrometer 32 acting as a wavelength-dispersive element makes it possible to collect data that is both wavelength-resolved and time-resolved. Figs 3a and 3b illustrate the experimental result of such a detection. It should be noted that the time scale in both Fig. 3a and Fig. 3b illustrate the intensity variation over time for one pulse only, although the actual data used for producing these figures is based on accumulated data from many readings. The time axis in Fig. 3a and 3b is in nano second scale.

Fig. 3a illustrates a streak camera image pasted into a time-wavelength diagram, the light portions correspond to high intensity values. The left part of the image corresponds to detected photons having a relatively short time delay, whereas the right part of the image corresponds to photons with a relatively long delay time.

The 3D plot in Fig. 3b corresponds to the image in Fig. 3a. This 3D plot clearly illustrates how the time-resolved spectroscopy according to the invention results in an intensity measurement as a function of both wavelength and photon propagation time. This 3D plot also clearly illustrate that the total information content as obtained by the present invention is significantly greater than the information obtainable with a conventional time-integrated detection.

In Fig. 3b, for each wavelength (such as for the wavelengths $\lambda 1$ and $\lambda 2$ as identified in Fig. 3b) there is a multitude of timely spaced intensity readings. Thus, for each wavelength it is possible to obtain a full curve of emitted (transmitted and/or reflected) intensity vs. propagation time. The form of these "time profiles" shown in Fig. 3b is dependent on the relation between the optical properties of the analysed sample. With such a time-resolved and wavelength-resolved spectroscopy, it is possible to obtain information for describing the light interaction with the sample. As an example, this provides the basis for determining an analyte concentration in a sample that is proportional to the absorption coefficient but not related to the scattering. As another example, one might want to measure an analytical quantity that correlates to the scattering properties of the sample instead.

As illustrated by the dashed lines t1 and t2 in Fig. 3b, it is also possible to evaluate the emitted light by detecting the intensity during fixed time slices. This would give a more coarse time resolution. In one embodiment, wavelength-resolved spectra are measured at two time gates only – one for "prompt" light and one for "delayed" light.

The intensity-time diagram in Fig. 5 illustrates two experimental, time-resolved results from measurements on two different tablets. By selecting suitable time gates where the difference is substantial, one can easily distinguish different tablets from each other.

As an alternative to the set-up illustrated in Figs. 1a and 1b, instead of using the water cuvette 20 in combination with he spectrometer 32, is possible to use wavelength selective light sources, such as diode lasers. On the detector side, wavelength selective detectors, such combinations of filters and detector diodes, can be used for each wavelength.

It is possible to combine the invention with a spatial-resolved intensity detection on the emitted light from the sample. In this context, the term "spatial resolved" refers to a spatial resolution obtained for each excitation pulse. Especially, "spatial-resolved" does not refer to a spatial resolution based on a scanning in time of the excitation beam in relation to the sample. As an illustrative example, by removing the water cuvette 22 and the spectrometer 32 in the Fig. 1a set-up, the light focused on the entrance slit of the streak camera would be spatial resolved along the slit, corresponding to a "slit" across the sample. A streak camera image obtained by such a set-up is illustrated in Fig. 4a, and a corresponding 3D plot is illustrated in Fig. 4b. In accordance with Figs 3a and 3b discussed above, Figs 4a and 4b represent one pulse only; i.e. the spatial resolution illustrated does not correspond to any scanning of the excitation beam over the sample.

CLAIMS

1. A method for use in quantitative analysis of a turbid, pharmaceutical sample (24), comprising the following steps:

- providing an excitation beam (20) of radiation;
- irradiating a pharmaceutical, turbid sample (24) with said excitation beam (20) of radiation; and
- detecting the intensity of emitted radiation (30) from the sample (24) as a function of both the wavelength of the emitted radiation and the photon propagation time through said sample (24).

2. A method as claimed in claim 1, wherein said emitted radiation comprises transmitted radiation (30) from said sample (24).

3. A method as claimed in claim 1, wherein said emitted radiation comprises diffusely reflected radiation (30') from said sample (24).

4. A method as claimed in claim 1, wherein said emitted radiation comprises transmitted radiation (30) as well as diffusely reflected radiation (20') from said sample (24).

5. A method as claimed in any of claims 1-4, wherein said excitation beam (20) is a pulsed excitation beam presenting a pulse train of excitation pulses (P), and wherein the step of detecting the intensity as a function of the photon propagation time is performed in time synchronism with said excitation pulses (P).

6. A method as claimed in claim 5, wherein said excitation pulses (P) have a pulse length shorter than the photon propagation time.

7. A method as claimed in claim 6, wherein said excitation pulses (P) have a pulse length selected short enough in relation to the photon propagation time such that any undesired interference between intensity measurements relating to two subsequent excitation pulses is prevented.

8. A method as claimed in any of claims 1-4, wherein said excitation beam (20) is an intensity modulated excitation beam.

9. A method as claimed in claim 8, wherein the step of detecting the intensity as a function of the photon propagation time is performed by comparing the phase of the intensity modulated excitation beam (20) with the phase of the emitted radiation (30) from the sample (24).

10. A method as claimed in claim 8 or 9, wherein the step of detecting the intensity as a function of the photon propagation time is performed by comparing the modulation depth of the intensity modulated excitation beam (20) with the modulation depth of the emitted radiation (30) from the sample (24).

11. A method as claimed in any of claims 1-10, wherein said detection of the intensity of emitted radiation (30) from the sample (24) as a function of time is performed by the use of a time-resolved detection unit.

12. A method as claimed in any of claims 1-10, wherein said detection of the intensity of emitted radiation (30) from the sample (24) as a function of time is performed by the use of a phase-resolved detection unit.

13. A method as claimed in any of claims 1-10, wherein said detection of the intensity of emitted radiation (30) from the sample (24) as a function of time is performed by the use of a time-gated system.

14. A method as claimed in any of the preceding claims, wherein said step of detecting the intensity further includes a spatial-resolved detection of said intensity.

15. A method as claimed in any of the preceding claims, wherein said pharmaceutical, turbid sample is a solid sample (24), in particular a tablet, a capsule, a bulk powder or an equivalent pharmaceutical dose.

16. A method as claimed in claim 15, wherein said step of irradiating the sample with said excitation beam comprises the step of irradiating a first surface of the solid sample (24).

17. A method as claimed in claim 15, wherein said step of irradiating the sample with said excitation beam (20) comprises the step of irradiating a first surface and a second surface of the solid sample (24), especially oppositely-directed surfaces.

18. A method as claimed in claim 17, wherein the first surface and the second surface of the solid sample are irradiated at different points in time.

19. A method as claimed in any of claims 1-14, wherein said pharmaceutical, turbid sample is a dispersion.

20. A method as claimed in any of the preceding claims, wherein the excitation beam (20) comprises infrared radiation.

21. A method as claimed in claim 20, wherein the infrared radiation is in the near infrared radiation (NIR).

22. A method as claimed in claim 21, wherein the radiation has a frequency in the range corresponding to wavelengths of from about 700 to about 1700 nm, particularly from 700 to 1300 nm.

23. A method as claimed in any of the preceding claims, wherein the excitation beam (20) comprises visible light.

24. A method as claimed in any of the preceding claims, wherein the excitation beam (20) comprises UV radiation.

25. A method for use in an analysis of turbid sample (24), wherein an excitation radiation is directed onto said sample (24) and wherein the intensity of emitted radiation (30) from the thus radiated sample (24) is measured as a function of both wavelength of the emitted radiation (30) and photon propagation time through said sample (24).

26. An apparatus for use in quantitative analysis of a turbid pharmaceutical sample (24), comprising:

- means (10, 12, 16) for generating an excitation beam (20) of radiation;
- means for positioning a pharmaceutical, turbid sample (24),
- means for focusing said excitation beam (20) onto said sample (24);
- means (32, 34, 36) for detecting the intensity of emitted radiation (30) from the sample (24) as a function of both the wavelength of the emitted radiation and the photon propagation time through said sample (24).

27. An apparatus as claimed in claim 26, wherein said means for detecting comprises a time-resolved detection unit (34).

28. An apparatus as claimed in claim 27, wherein said time-resolved detection unit comprises a streak camera (34).

29. An apparatus as claimed in claim 26, wherein said means for detecting comprises a phase-resolved detection unit.

30. An apparatus as claimed in claim 26, wherein said means for detecting comprises a time-gated system.

31. An apparatus as claimed in any of claims 26-30, further comprising means for performing a spatial-resolved detection of said intensity.

32. An apparatus as claimed in any of claims 26-31, wherein said pharmaceutical, turbid sample is a solid sample (24), in particular a tablet, a capsule, a bulk powder or an equivalent pharmaceutical dose.

33. A apparatus as claimed in any of claims 26-31, wherein said pharmaceutical, turbid sample is a dispersion.

34. An apparatus as claimed in claim 26, wherein the excitation beam (20) comprises infrared radiation.

35. An apparatus as claimed in claim 34, wherein the infrared radiation is in the near infrared radiation (NIR).

36. An apparatus as claimed in claim 26, wherein the radiation has a frequency in the range corresponding to wavelengths of from about 700 to about 1700 nm, particularly from 700 to 1300 nm.

37. An apparatus as claimed in any of claims 26-36, wherein the excitation beam (20) comprises visible light.

38. An apparatus as claimed in any of claims 26-37, wherein the excitation beam (20) comprises UV radiation.

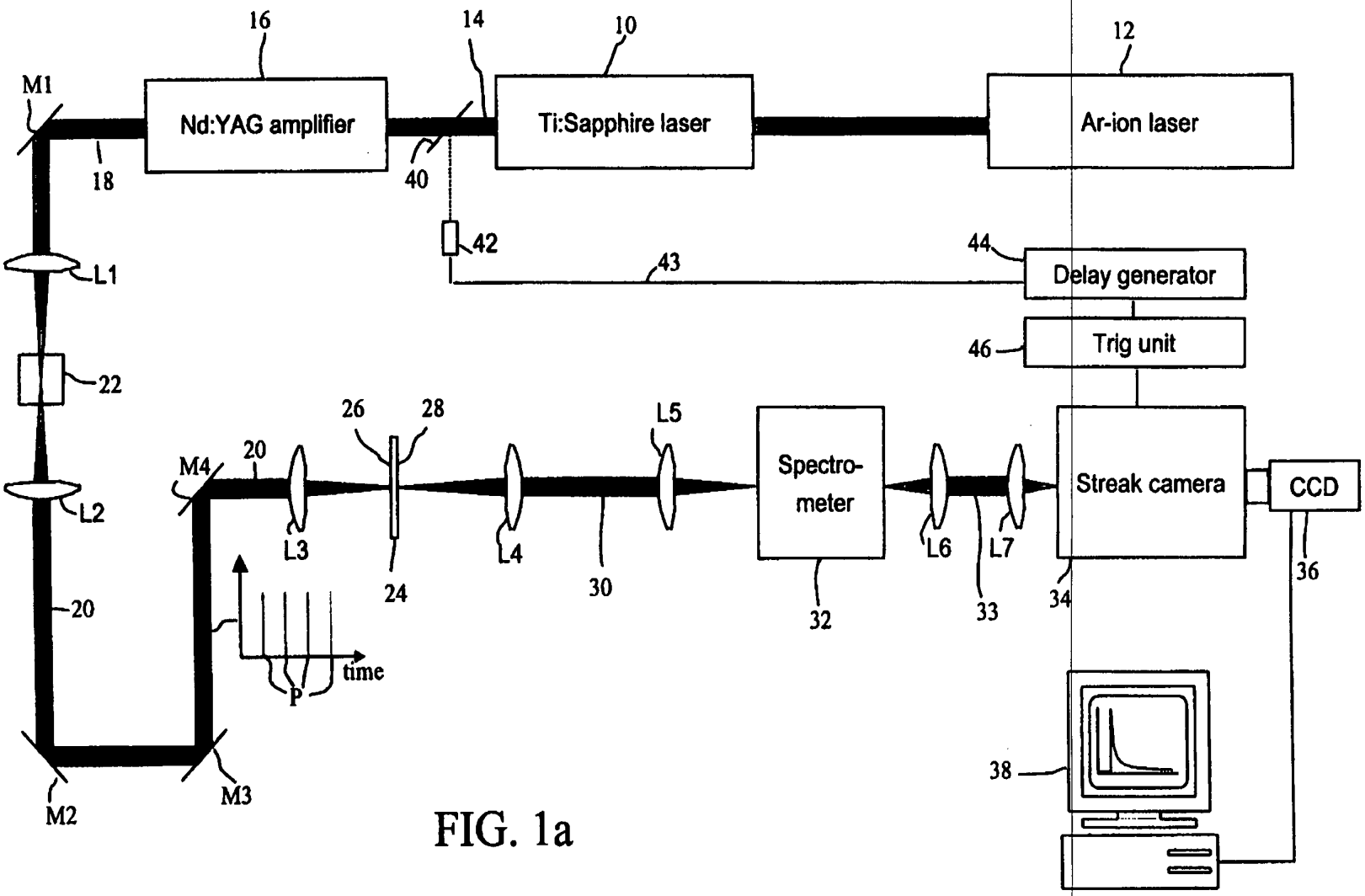
39. An apparatus as claimed in any of claims 26-38, wherein said means (10, 12, 16) for generating comprises one or more diode lasers.

40. An apparatus as claimed in any of claims 26-38, wherein said means (10, 12, 16) for generating comprises an intensity modulated lamp.

PRIOR ART

ABSTRACT

The present invention relates to a method and an apparatus for use in performing a quantitative analysis of a turbid pharmaceutical sample, e.g. a tablet, a capsule or a similar sample forming a pharmaceutical dose. A pharmaceutical, turbid sample (24) is irradiated with an excitation beam (20) of radiation, e.g. near infrared radiation. The intensity of emitted radiation (30) from the sample (24) is detected as a function of both the wavelength of the emitted radiation and the photon propagation time through said sample (24). Optionally, the intensity of the emitted radiation (30) from the sample (24) is also detected in a spatially resolved manner.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Delay generator
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Trig unit
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26
28
L5
20
M4
Spectro-
meter
Streak camera
CCD
L2
L3
L4
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M3

FIG. 1a

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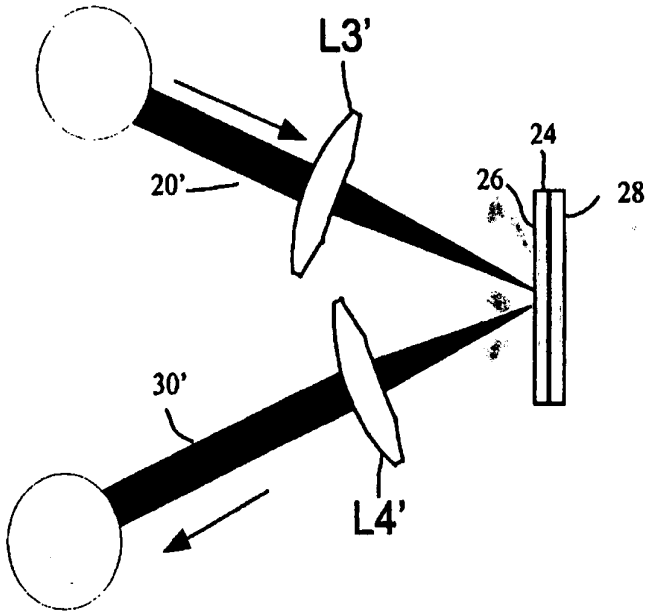

FIG. 1b

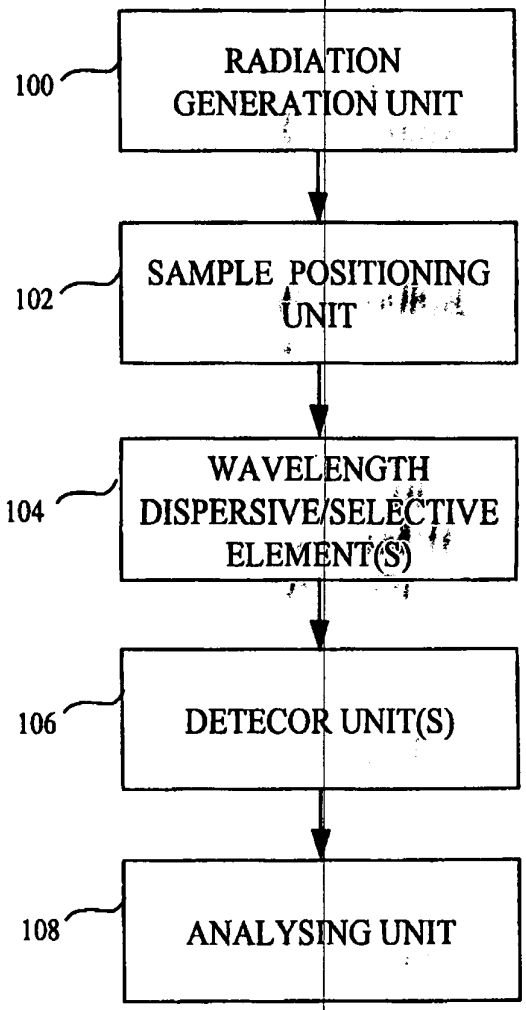

FIG. 2

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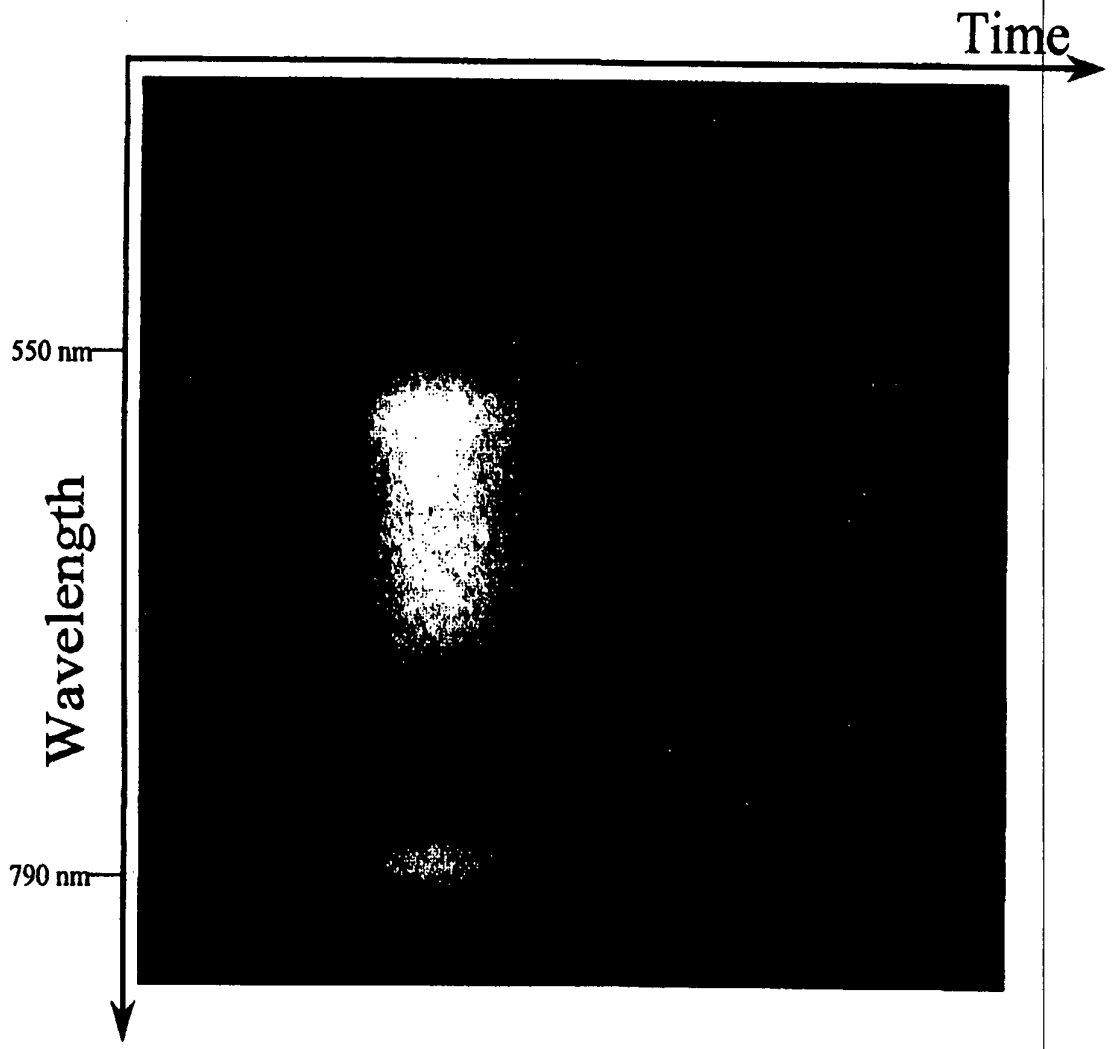

FIG. 3a

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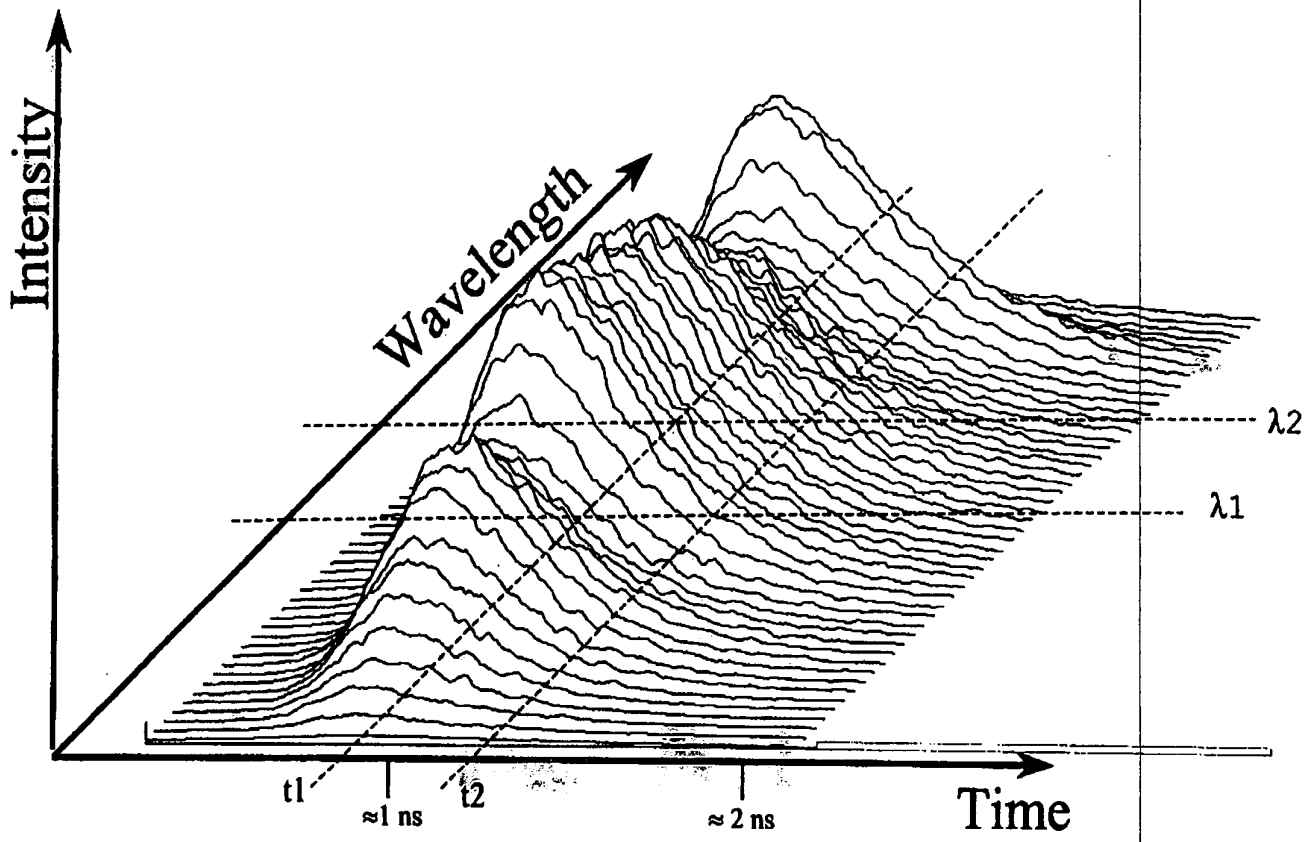
3D plot of image data in Fig. 3a.

FIG. 3b



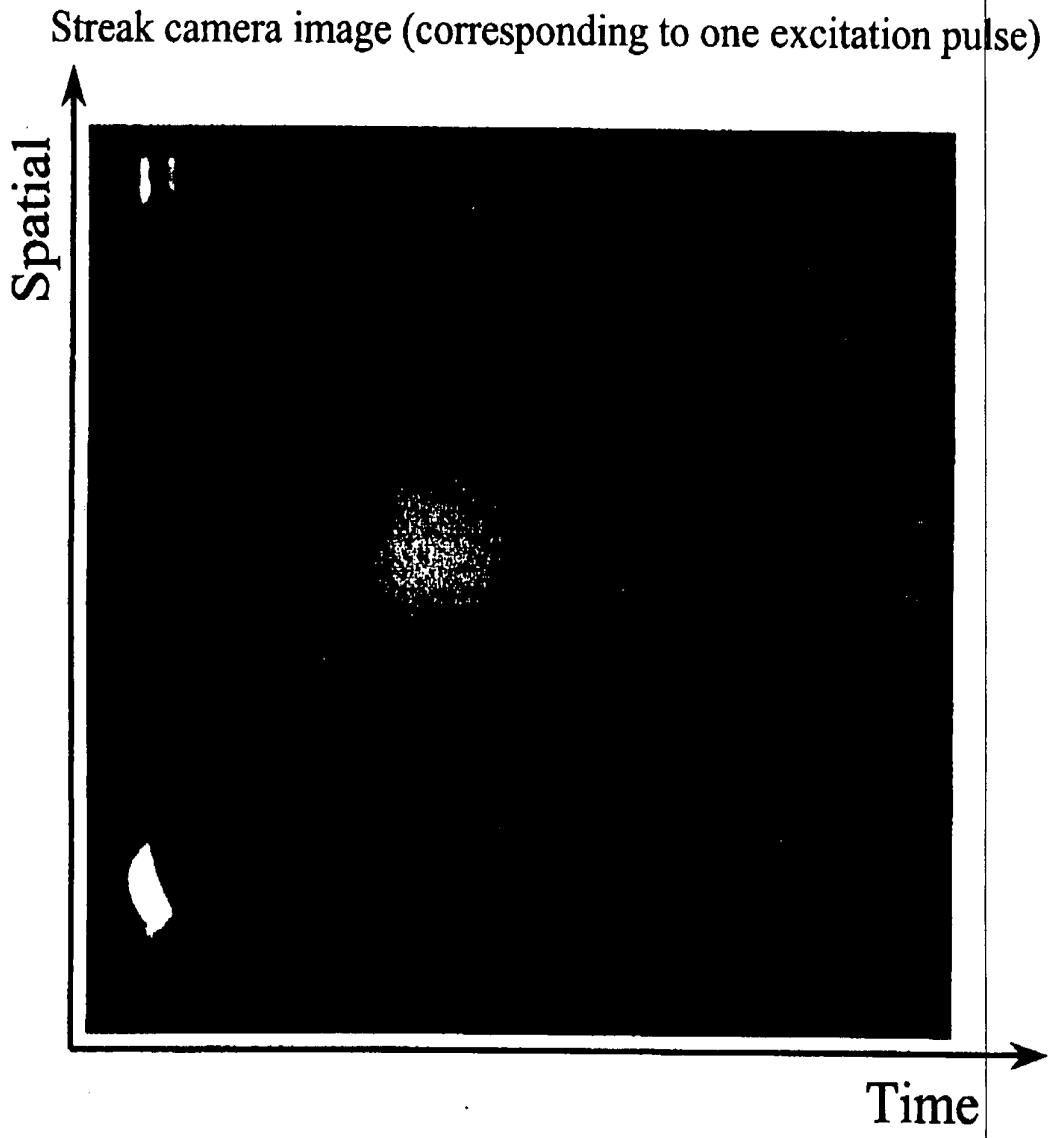

Streak camera image (corresponding to one excitation pulse)
Spatial
Time

FIG. 4a

990423--3

3D plot of image data in Fig. 4a

FIG. 4b

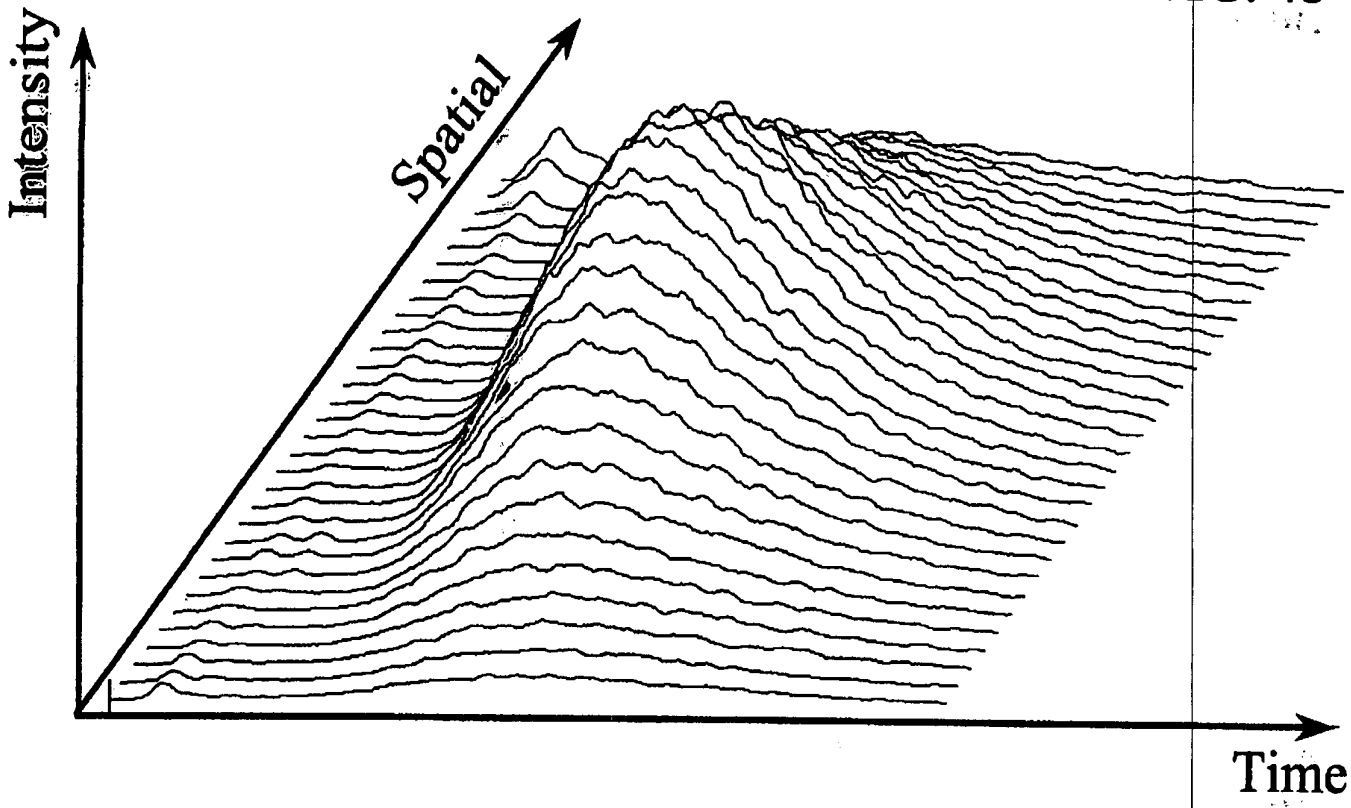
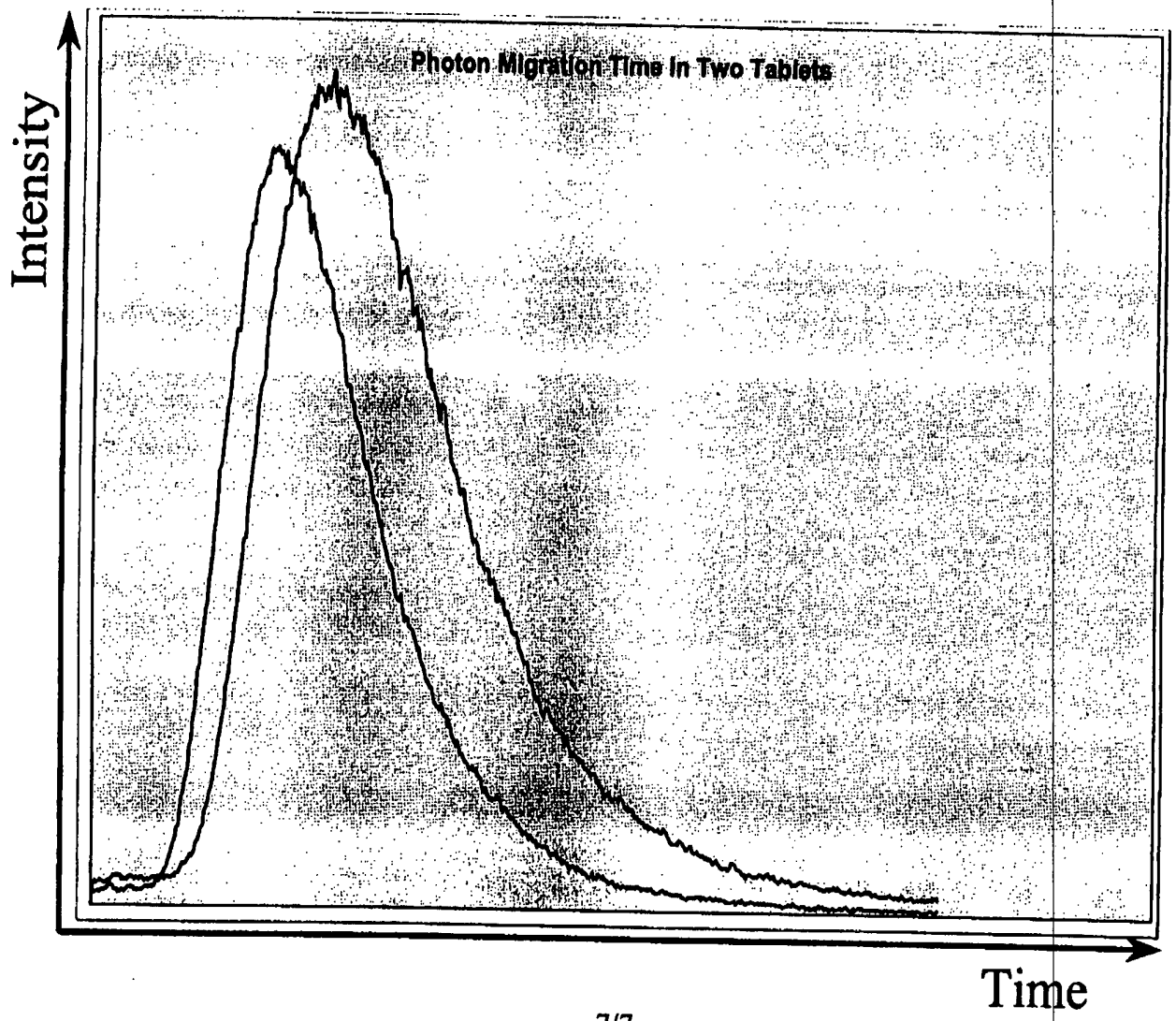


FIG. 5



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